protein or polypeptide to be synthesized and chemically linking the amino acids in an orientation and under suitable conditions so as to produce the protein or polypeptide.

II. REMARKS

Claims 1-30 are pending in this application. Claims 7-19, 21, 22 and 25 to 30 were withdrawn from examination as a result of a restriction requirement. Claims 1-6, 20, 23 and 24 are under examination. In the outstanding Office Action, the disclosure and specification are objected to. Claim 1 stands rejected as allegedly drawn to non-patentable subject matter and claims 1, 2, 4, 5, 6, 20, 23 and 24 stand rejected under 35 U.S.C. § 112, first and second paragraphs. Claims 1 through 6 and 20 stand rejected under 35 U.S.C. § 103.

By this paper, the specification and claims have been amended. Support for the amendments to the specification can be found in the Figures as originally filed and in the Sequence Identification Listings filed on March 11, 1996. Support for the amendment to claim 1 can be found, for example, on page 13, line 22 to 25. Support for the amendment to claims 23 and 24 can be found on page 17. Support for new claim 31 through 36 can be found, for example, on page 9, lines 16 to 24 and in Example XI which describes non-naturally occurring FADD muteins FADDmt and AU1-N-FADD. No new matter is added as a result of these amendments, and entry thereof is respectfully requested. Amended claims 1 to 6, 20, 23, 24 and newly added claims 31 to 36 are presently under examination.

In view of the preceding amendments and the remarks that follow, reconsideration and withdrawal of the objections to the specification and the rejection of the claims are respectfully requested.

Informalities

The disclosure is objected to because the Brief Description of the Drawings is allegedly not to recite SEQ ID NOs identifying the sequences shown in Figures 2A and 2B. In addition, it

is asserted that the application fails to comply with the requirements of 37 C.F.R. § 1.821 to 1.825 and the specification contains a number of separate sequences encoding or representing peptides that refer to the sequence in Figure 2A.

To help resolve these issues, Applicants would like to clarify the status of the documents previously submitted in this case. The Office Action states that amendments filed on 22 February 1996 were entered. However, Applicants have no record of amendments submitted on that date. On February 5, 1996, the Office acknowledged receipt of an Information Disclosure Statement, a PTO-1449 and accompanying references. On March 11, 1996, the Patent Office received a "Statement to Support Filing and Submission in Accordance with C.F.R. Sec. 1.821-1.825" along with a "Response to Notice to Comply with Requirements for Patent Applications Containing Nucleotide Sequence Disclosure" and a diskette containing the SEQ ID listings. The response corrected three sequence listings inadvertently omitted and provided substitute listings.

With respect to the references in the specification to nucleotide and amino acid sequences, Applicants have herein amended their specification to identify these sequences by their SEQ ID NO identifier in the proper format. The specification fully complies with 37 C.F.R. § 1.821-1.825 and the informalities have all been corrected.

Restriction Requirement

The Examiner has required restriction to one of the following allegedly independent and distinct inventions under 35 U.S.C. § 121:

Group I: Claims 1-6, 21, 23 and 24, drawn to proteins and polypeptide fragments;

Group II: Claims 7-14, 20 and 22, drawn to nucleic acids, compositions containing nucleic acids, and processes for making FADD protein and chemically replicating nucleic acid molecules.

Group III: Claims 15, 16, and 19 drawn to antibodies, nucleic acids encoding antibodies and hybridomas.

Group IV: Claims 17 and 18, drawn to an agent which has the ability to inhibit binding and an agent that inhibits Fas-associated apoptotic cell death.

Group V: Claim 21, drawn to a process for chemical synthesis of a FADD protein.

Groups VIa/VIb: Claims 25 and 26, drawn to a method modulating cellular function.

Group VII: Claim 27, drawn to a method of modulating cellular function.

Group VIII: Claim 28, drawn to a method of maintaining T-cell viability.

Group IX: Claims 29 and 30, drawn to assay methods for screening an agent.

The Office states that the inventions are distinct and require an election of one of the Groups. During a telephone conference on June 7, 1996, Applicants' undersigned attorney made a provisional election of Group I (claims 1-6, 21, 23 and 24) with traverse. Applicants herein confirm the election of Group I with traverse. Applicants expressly reserve the right under 35 U.S.C. § 121 to file one or more divisional applications directed to the nonelected subject matter during the pendency of this application.

Applicants respectfully request that the Examiner reconsider and withdrawn the requirement for restriction as between Groups I (claims 1-6, 21, 23 and 24), Group IV (claims 17 and 18), Group V (claim 21) and Group IX (claims 29 and 30), and examine these claims in this case.

A restriction requirement is proper only if the Office shows that two criteria have been satisfied: (1) the inventions must be independent and distinct and (2) there must be serious burden imposed on the Examiner if restriction is not required. (MPEP § 808). Therefore, the Examiner must examiner the subject application on its merits, even though it includes claims to distinct invention, if the search and examination of the application can be made without serious burden.

Applicants submit that it would not impart a serious burden on the Examiner to examiner Groups I, IV, V and IX together. Group I is directed to FADD proteins; Group IV to agents which inhibit FADD protein binding; Group V to a process of synthesizing FADD proteins and

Group IX to methods of screening for agents which modulate cellular function using a FADD protein. All of the inventions of these Groups, therefore, involve a search of the art for FADD proteins, and a search for these proteins would certainly reveal inhibitory agents, methods of synthesis and methods of screening. Thus, it would not impart a serious burden on the Examiner to search these Groups together.

The Examiner states that Group I (claims 1-6, 21, 23 and 24) and V (claim 21) are patentably distinct between the product of Group I is made by a materially different method of producing the protein. Similarly, Group I is alleged to be distinct from about IV because the inhibitory agents could be used for a materially different purpose. Applicants respectfully point out that claim 21 has been already classified by the Examiner as belonging to either Group I or Group V, and both Groups share the same classification, class 530. Furthermore, Groups I and IV are related in that the invention of Group IV requires use of a FADD protein to determine inhibition, and, accordingly, depends on claim 1 of Group I. In view of the close interrelatedness of the claimed inventions, it would not impart a serious burden on the Examiner to search and examiner the inventions of Group I, IV and V together, especially in view of the double classification of Group V by itself or with Group I. (See, Office Action, page 3, line 3 and page 7, line 20).

The inventions of Group IX (claims 29 and 30) and Group I (claims 1-6, 21, 23 and 24) are alleged to be unconnected in design, operation and effect. Applicants submit that Group IX requires the use of a detectably labeled FADD protein and are thus, at the very least, related in design. Groups IV and V are similarly related to Group IX as synthesized FADD proteins and use of these proteins.

Applicants maintain, therefore, that the neither criteria of MPEP § 808 has been met with respect to Groups I, IV, V and IX. In particular, the inventions of these Groups are not independent and distinct nor would it impart a serious burden on the Examiner to search these Groups together. Accordingly, the restriction requirement as between Groups I, IV, V and IX is improper, and Applicants request that it be withdrawn.

35 U.S.C. § 101

Claim 1 stands rejected under 35 U.S.C. § 101 as allegedly encompassing products of nature. Without conceding the correctness of the Examiner's position, Applicants have amended claim 1 to specify that the protein is "an isolated FADD protein." Support for this amendment can be found on page 13, lines 22 to 25. New claim 31 specifies that the FADD protein is not naturally occurring. Thus, in view of these amendments, this rejection has been obviated.

35 U.S.C. § 112, First Paragraph

Claims 1 to 6, 20, 23 and 24 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly not enabled by the specification. In particular, it is alleged that disclosure is enabling only for the Fas-associated death domain (FADD) proteins identified in SEQ ID NO:2. It is alleged that the specification does not provide a physical description of each protein capable of functioning as the claimed protein.

Under 35 U.S.C. § 112, first paragraph, the specification must teach one of skill in the art how to make and use the claimed invention. *In re Wright*, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). Not everything necessary to practice the invention need be disclosed. In fact, what is well-known in the art is preferably omitted from the specification. *Cf. Hybritech Inc., v. Monoclonal Antibodies, Inc.*, 231 USPQ 81, 94 (Fed. Cir. 1986), *cert. denied,* 480 U.S. 947 (1987).

Applicants submit that the specification fully enables claims 1 to 6, 20, 23, 24 and 31 to 36. Claim 1 has been amended herein to recite "an isolated FADD protein." Independent claims 6 and 20 also specify the claimed protein is a FADD protein or polypeptide. Claim 31 recites a non-naturally occurring FADD protein. Thus, the specification must teach a skilled artisan how to make and use a FADD protein.

The specification defines FADD in both structural and functional terms. FADD proteins are characterized as having biological or functional ability to modulate cellular function

associated with the Fas receptor pathway, including apoptosis. (See, page 13, lines 22 to 25.) On page 14, line 29 to page 15, line 7, the specification defines purified FADD as a 208 amino acid molecule with an apparent molecular weight of about 23.3 kD and as having a "death domain" sequence shown in SEQ ID NO:1. Thus, the specification provides a clear physical description of the claimed molecules, and a skilled artisan could, therefore, readily make and use the claimed FADD proteins. Withdrawal of this rejection is requested.

Claims 3 to 5 also stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly not enabled by the specification. The Office asserts that the specification does not provide adequate guidance to make and use the claimed polypeptide fragments. Claim 3 is drawn to a fragment of the FADD protein, claim 4 is directed to a polypeptide which includes the C-terminal portion of FADD and claim 5 is drawn to the N-terminal portion of a FADD protein which induces apoptosis in a suitable cell. Similar claims have been added for non-naturally occurring FADD polyeptides (See claims 32–35).

Applicants submit that the specification provides ample guidance on how to make and use the polypeptides of claims 3 to 5 and 32 to 35. On page 15, line 7 through page 16, line 16, Applicants' specification teaches how several different fragments of FADD can be used. Moreover, on page 16, line 28 through page 17, line 29, the specification describes how FADD fragments can be made, using methods well-known in the art. Exemplary amino acid sequences are provided throughout the specification. Furthermore, on page 50, lines 9-14, Applicants demonstrate how N-terminal and C-terminal FADD fragments were actually made and how they function. The C-terminal fragment of claim 4 is described in detail, for instance, on page 50, lines 11 to 14 and the N-terminal fragment of claim 5 is described on page 53, lines 1 to 18. Thus, armed with the subject specification, a skilled artisan could readily make and use fragments of the FADD protein, including a C-terminal fragment and an N-terminal fragment. Accordingly, the specification fully enables claims 3 to 5 and 32–35, and Applicants' respectfully request withdrawal of the outstanding § 112, first paragraph rejection.

35 U.S.C. § 112, Second Paragaraph

Claim 24 stands rejected under 35 U.S.C. § 112, second paragraph as allegedly indefinite for reciting a protein or polypeptide produced by claim 22 which is directed to a process of producing nucleic acids. By amendment herein, claim 24 has been amended to recite a nucleic acid produced by the process of claim 36. Support for this amendment can be found on page 21, lines 4 to 11. Therefore, this rejection has been rendered moot and Applicants request that it be withdrawn.

35 U.S.C. § 103

Claims 1 to 6 and 20 stand rejected under 35 U.S.C. § 103 as allegedly obvious over Itoh *et al.* (1983) in view of Maekawa *et al.* (1991) and in further view of Morrison *et al.* (1989). The Examiner alleges that Itoh teaches the amino acids of the cytoplasmic region of the Fas antigen responsible for apoptosis, known as the death domain, but does not teach a purified mammalian polypeptide or fragment capable of inducing apoptosis. Maekawa is cited for teaching the cloning and expression of a protein that binds the cytoplasmic region of a Fas antigen (PTP-BAS). Morrison is cited as teaching the purification of a protein that binds to the cytoplasmic regions of tyrosine kinase receptors, including the Fas receptor. It is alleged that it would have been obvious to one of skill in the art to use the method of Morrison to purify Maekawa's protein and that Maekawa's protein could be expressed in a host cell using the method of Itoh.

Applicants strongly disagree that the present invention is rendered obvious by the combination of the cited references. Pursuant to 35 U.S.C. § 103, the cited references must teach or suggest each element of the claimed invention. Indeed, the public policy of the patent system, articulated in the last sentence of § 103, serves to prevent serendipitous discoveries from receiving preference over careful, methodical research and development strategies by not allowing rejections based on "an obvious to try" standard. *In re Lindell,* 155 USPQ 521, 523 (CCPA 1967). Thus, it is improper to reject claims to specific molecules based on an alleged

obviousness of a method of making the molecules. *In re Deuel*, 34 USPQ2d 1210 (Fed. Cir. 1995).

In *Deuel*, the PTO rejected claims to specific cDNA sequences and nucleotide sequence covering heparin-binding growth factor based on references which disclosed the N-terminal portion of a brain-specific heparin binding growth factor and a reference describing a general method for gene cloning once partial amino acid sequence was known. The Federal Circuit reversed this rejection, holding that a general motivation to search for a gene known to exist but not defined in combination with a general method of probing for such a gene does not make obvious a specifically-defined gene that is subsequently obtained. *Id.* at 1216. Therefore, because the references cited in *Deuel* did not teach or suggest the specific claimed molecules, a rejection based on § 103 was improper.

The facts of the pending application are analogous to those in *Deuel.* As acknowledged by the Examiner, the cited references do not teach or suggest the claimed sequences. Thus, as in *Deuel*, the Office is attempting to show obviousness of the specifically claimed sequences by relying on general methods (Morrison and Itoh), a partial C-terminus amino acid sequence of a distinct protein (Maekawa) and a protein which binds to the claimed molecules (Itoh). The court in Deuel clearly held that the teachings of such references cannot establish a *prima facie* case of obviousness. Applicants request withdrawal of this rejection.

Initialled PTO Forms 1449

Applicants acknowledge receipt of the Examiner-initialled PTO 1449 Forms filed with the Information Disclosure Statement received by the Office on February 5, 1996.

Drawings Objection

Applicants also acknowledge receipt of the PTO 948 Form enclosed with the outstanding Office Action. Drawings corrected to overcome the alleged informalities will be filed prior to the payment of the issue fee.

III. CONCLUSION

If a telephone interview would be of assistance in advancing prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided below.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, Applicants petition for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952 (Ref. No. 20344-21070.20)**. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: January 17, 1997.

Respectfully submitted,

By: _____

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